

Remarks

Claim Amendments

Claims 6, 7, 14, 15, 18 and 19 have been canceled herein without prejudice to their filing in divisional or continuation applications. Pursuant to this amendment, the current status of the claims is shown in the Claims Listing above.

Obviousness

Claims 1-3, 5, 8-13, 16-17 and 20 are nonobvious and patentable over the '903 patent in view of Weber. The rejection of these claims over the cited art relies upon the proposition that "the prior art teaches a species of a binding pair that meet the expected characteristics of the prior art contemplated binding pair" (Office Action at page 4, lines 12-13). That is to say that the prior art of Weber teaches a binding pair (biotin-avidin) that meets the characteristics of the binding pair contemplated by the '903 patent. Applicants respectfully submit that a careful reading of both Weber and the '903 patent reveals that the binding pair of Weber (biotin-avidin) does not meet the characteristics of the binding pair contemplated by the '903 patent.

The '903 patent teaches both binding pairs that interact non-covalently and covalently. When referring to binding pairs that interact non-covalently (as in Applicants claimed invention), the '903 patent states that "Whenever the interaction of X and Y is based on the formation of stable hydrophobic complex, X and Y are lipophilic groups." No other type of non-covalent interaction between the members of the binding pair are contemplated by the '903 patent. Only when referring to covalent interactions does the '903 patent state that "Preferably, whenever X and Y form a covalent linkage, or bridge, X and Y pairs must react specifically with each other when brought into juxtaposition, but otherwise they must be substantially unreactive with chemical groups present in a cellular environment."

Focusing, then, on the non-covalent binding pair contemplated by the '903 patent (as in Applicants claimed invention), it is a lipophilic group. The term "Whenever" leaves no room for anything else. The binding moiety (biotin-avidin) of Weber is not a lipophilic group, and as taught by Weber, it does not meet the characteristics of a lipophilic group. Specifically, Weber teaches that "localization of negative charge on the biotin ureido oxygen is reflected by its

tetrahedral (sp^3) coordination to three protein side chains that donate hydrogen bonds and form an oxyanion pocket for the ureido oxygen.” (page 3198, second column, lines 21-24) Weber further teaches that “the dominant effect contributing to biotin binding is enhanced hydrogen bonding made between the ligand and protein due particularly to stabilization of a biotin resonance form whose tetrahedrally coordinated, sp^3 ureido oxygen makes more and stronger hydrogen bonds than an sp^2 oxygen forms with water in solution.” (page 3198, second column, lines 39-44).

As one skilled in the art will recognize, a lipophilic group is a hydrophobic group, that is, it acts through non-polar interactions. As taught by Weber, biotin and avidin bind through highly polar hydrogen bonding, made even stronger by the tetrahedrally coordinated sp^2 ureido oxygen of biotin in the binding pocket. Thus, the binding pair taught by Weber is not a lipophilic group, as contemplated by the ‘903 patent, nor does it “meet the characteristics” of a lipophilic group, as required by the Examiner’s own rejection.

For these reasons, Applicants respectfully submit that it is not appropriate to substitute the strong hydrogen bonding pair taught by Weber with the relatively weak lipophilic binding pair contemplated by the ‘903 patent. Accordingly, Applicants respectfully request that this rejection of claims 1-3, 5, 8-13, 16-17 and 20 be withdrawn.

Anticipation

Claims 18 and 19 have been canceled. Therefore, this rejection is rendered moot.

Obviousness-type Double Patenting

Claims 18 and 19 have been canceled. Therefore, this rejection is rendered moot.

Conclusion

Claims 1-3, 5, 8-13, 16-17 and 20 are now believed to be patentable over the prior art. Applicants earnestly solicit early notification to this effect. If the Examiner believes that any discussion of this communication would be helpful, the Examiner is invited to contact the undersigned attorney by telephone at 781-933-6630.

Respectfully submitted,

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